REMARKS

Reconsideration of the present application in view of the present amendments and the following remarks is respectfully requested. Claims 75-84 and 104 are currently pending in the instant application. Claims 75, 83, 84, and 104 have been amended and new claims 113-123 have been added to define more clearly certain subject matter of Applicants' invention. Support for the amended and new claims may be found in the specification, for example, at page 7, lines 18-22; page 15, lines 19-28; page 18, lines 1-6; page 19, lines 19-27; page 22, line 22 through page 26, line 27; page 31, lines 4-18; page 34, lines 1-24; page 40, lines 3-19; page 54, line 10 through page 55, line 17; and page 55, line 28 through page 56, line 8. No new matter has been added.

REJECTIONS UNDER 35 U.S.C. § 102(b)

Claim 104 stands rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Neumann et al. (*J. Immunol.* 152:343 (1994)). More specifically, the Action asserts that Neumann et al. disclose 96-well ELISA plates comprising an immobilized ANT polypeptide for screening of candidate agents that bind to an ANT polypeptide, and that the immobilized ANT polypeptides of Neumann et al. are patentably indistinguishable from recombinant ANT polypeptides and are considered variants of recombinant ANT polypeptides of other isoforms.

Applicants respectfully traverse this rejection and submit that the PTO has not established a *prima facie* case of anticipation because Neumann et al. fail to teach each and every element of the instant claim. Applicants' invention is directed in pertinent part to a multi-well assay plate for high throughput screening, each well of which comprises at least one immobilized recombinant ANT polypeptide selected from human ANT1 as set forth in SEQ ID NO:31 or a variant thereof which comprises an amino acid sequence at least 95% identical to SEQ ID NO:31, human ANT2 as set forth in SEQ ID NO:32, and human ANT3 as set forth in SEQ ID NO:33.

Applicants submit that Neumann et al. fail to teach or suggest the presently claimed assay plate. Neumann et al. merely describe coating wells of a 96-well plate with non-recombinant bovine ANT isolated from bovine cardiac tissue. Bovine ANT polypeptides are

structurally distinct from the presently recited recombinant human ANT polypeptides. Neumann et al. fail to disclose *a priori* the desirability of coating multi-well plates with human ANT polypeptides as recited by the instant claim, to the exclusion of the myriad possible highly conserved ANT polypeptides from any other species. Moreover, Neumann et al. fail to suggest the desirability of immobilizing ANT for high-throughput screening or the desirability therefor of recombinant ANT, for reasons discussed in Applicants' response previously made of record.

Accordingly, Applicants submit that the subject matter recited in claim 104 is novel, meeting the requirements under 35 U.S.C. § 102(b), and respectfully request that this rejection be withdrawn.

Claim 83 stands rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Roux et al. (*Anal. Chem.* 234:31-37 (1996)). More specifically, the Action asserts that Roux et al. disclose a method comprising contacting an agent (a fluorescent atractyloside derivative that binds ANT) with a biological sample that contains ANT, and detecting binding of the agent, where the sample includes an ANT polypeptide that is at least 95% identical to SEQ ID NO: 32 or 33.

Applicants respectfully traverse this rejection and submit that Roux et al. fail to disclose each element of the present invention and therefore fail to anticipate the instant claim. Roux et al. fail to teach or suggest a method comprising culturing a recombinant host cell to produce a biological sample comprising a recombinant ANT polypeptide, nor do Roux et al. teach a recombinant expression construct comprising at least one regulated promoter operably linked to a nucleic acid encoding an ANT polypeptide as presently recited. Roux et al. also fail to teach or suggest identifying an ANT-binding agent by contacting a candidate agent with such a biological sample comprising a recombinant ANT polypeptide. Roux et al. merely disclose contacting N-ATR or Mant-ATR with beef heart mitochondria to detect bovine ANT, but Roux et al. in no way contemplate the use of any recombinant ANT, much less the recited recombinant ANT polypeptides. As discussed above, the amino acid sequence of bovine ANT is not identical to any one of the amino acid sequences of human ANT1, human ANT2, or human ANT3, as set forth in SEQ ID NOS: 31, 32, or 33, respectively, and is less than 95% identical to

the amino acid sequence of human ANT1 (SEQ ID NO:31). Applicants therefore submit that Roux et al. fail to anticipate the subject matter of claim 83.

Accordingly, Applicants submit that all claims meet the requirements for novelty under 35 U.S.C. § 102 and respectfully request that these rejections be withdrawn.

REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH (ENABLEMENT)

The PTO rejects claims 75-84 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The PTO concedes that the specification enables a method for identifying an agent that binds to ANT, wherein the method comprises contacting the candidate agent with a host cell expressing an ANT fusion protein having a polypeptide fused to the ANT N-terminus, and wherein the ANT polypeptide comprises at least 95% identity to SEQ ID NOS: 31, 32, or 33. The PTO alleges, however, that undue experimentation would be required to express recombinant non-fusion ANT polypeptides that have the claimed amino acid sequences and that would be able to bind other proteins.

Applicants respectfully traverse these rejections and submit that as disclosed in the present specification and recited in the instant claims, Applicants fully enabled the claimed invention at the time the application was filed. Applicants' invention is directed in pertinent part to a method for identifying an agent that binds to an ANT polypeptide, comprising contacting a candidate agent with a biological sample (*e.g.*, a host cell) that comprises an ANT polypeptide, as recited, which is recombinantly expressed using a regulated promoter.

Contrary to the PTO's assertions, the instant claims are commensurate in scope with the disclosure of the specification, which enables a skilled artisan to practice the invention readily and without undue experimentation. The specification describes methods for making recombinant full-length human ANT polypeptides using recombinant expression constructs that have a regulated promoter operably linked to the nucleic acid encoding the ANT polypeptide (*see, e.g.,* page 14, lines 21-28; page 15, lines 19-28; pages 61-74 (Example 1)). Thus, for example, according to the specification the nucleic acid may include (i) *only* the coding sequence for the ANT polypeptide (*e.g.,* SEQ ID NOS: 31, 32, or 33); (ii) the *coding sequence* for the ANT polypeptide *and additional coding sequence*; or (iii) *coding sequence* for the ANT

polypeptide and *non-coding sequence* (*e.g.,* page 20, lines 14-30; page 23, line 26 through page 24, line 8).

As conceded by the PTO, the specification teaches how to make and use a recombinant expression construct that encodes a fusion protein comprising at least one promoter operably linked to a nucleic acid molecule comprising a first nucleic acid molecule that encodes a first polypeptide and a second nucleic acid molecule that encodes a human ANT3 polypeptide having an amino acid sequence at least 95% identical to SEQ ID NO:33 (*see, e.g.,* page 22, line 22 through page 27, line 29). The specification also teaches that polypeptide sequences, for example, polyhistidine, immunoglobulin constant region, protein A, streptavidin or a GST polypeptide, fused to an ANT polypeptide, may be useful for facilitating detection, localization, and/or isolation of ANT (*see, e.g.,* page 25, lines 12-25; page 26, lines 13-27; *see also* Examples 1 and 2).

Contrary to the assertion by the PTO, however, the specification is not so limited as to teach that recombinant ANT polypeptide expression in a host cell will be achieved *only* when a recombinant expression construct comprises a nucleotide sequence that encodes non-ANT sequences at the amino terminal end of an ANT polypeptide. The specification thus teaches that such non-ANT sequences useful for purification and isolation may also be fused to the carboxy terminus of an ANT polypeptide (*see, e.g.,* page 25, line 23 through page 26, line 27, including references cited therein; *see, e.g.,* page 5, lines 18-20). These non-ANT polypeptide sequences, as described in the specification, are well known in the art for use as fusion protein domains, for example, to aid in the isolation and/or purification of a polypeptide of interest (*see, e.g.,* page 25, line 23 through page 27, line 7).

As also noted above, the specification clearly teaches that the subject invention recombinant expression construct may comprise a regulated promoter operably linked to a nucleic acid encoding an ANT polypeptide as recited, *without* the nucleic acid comprising any additional polypeptide encoding sequence. Applicants are somewhat puzzled by the assertion made by the PTO that "undue experimentation would be required to develop recombinant expression of *non-fusion* ANT polypeptides having the claimed sequences that would be active (able to bind other proteins)" (Action, at page 8, last paragraph, emphasis added). Specifically, in Example 4 (pages 83-87 and Figure 10) the specification describes recombinant expression in

yeast of human ANT3 polypeptides by themselves, and not as fusion proteins (*see e.g.*, page 86, lines 6-7: " . . . huANT3 produced from the yeast expression constructs lacks an epitope tag . . .").

In view of the foregoing, Applicants disagree with the PTO's assertion that undue experimentation would be required to practice the claimed invention. As just noted, the specification not only provides clear and abundant guidance with regard to how recombinantly to express unmodified ANT polypeptides, but further provides a working example of such an invention embodiment.

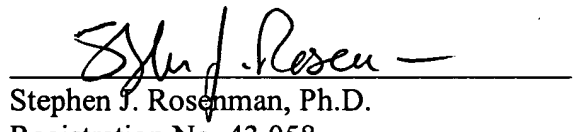
The PTO therefore errs in its assertion that addition to or replacement of human ANT polypeptide specific amino terminal sequences is *required* for expression of an ANT polypeptide in a recombinant expression system, based on the results described in Hatanaka et al. years after the filing date of the present application (*Biol. Pharm. Bull.* 24:595-99 (2001)). Hatanaka et al. were unable to express human ANT (AAC1) specific RNA in the yeast recombinant expression system disclosed therein unless nucleotides encoding human ANT amino terminal amino acids were replaced with nucleotides encoding yeast ANT amino terminal amino acids (*see* Hatanaka et al., Figure 3). Hatanaka et al. did not, however, employ a regulated promoter, which is a feature of the instant claims (see, *e.g.,* Hatanaka et al. at page 598, right-hand column, second paragraph, first sentence). By contrast, in the present application Applicants have provided a working example showing recombinant human ANT expression in a (heterologous) yeast recombinant expression system using a non-fusion construct, *i.e.*, without modifying the ANT-encoding nucleic acid by any addition and/or substitution of nucleotide sequences encoding any amino terminal polypeptide sequence (*see* page 83, line 13 through page 86, line 3).

Applicants therefore respectfully submit that the present specification provides ample guidance enabling a person skilled in the art to make and use the entire breadth of the claimed invention, readily and without undue experimentation. Accordingly, Applicants respectfully submit that the Application satisfies the requirements for enablement under 35 U.S.C. § 112, first paragraph, and request that this rejection be withdrawn.

Applicants respectfully submit that all claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned representative at 206-622-4900.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



Stephen J. Rosenman, Ph.D.
Registration No. 43,058

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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